PREVALENCE OF MICROALBUMINURIA IN NORMOGLYCAEMIC - NORMOTENSIVE OBESE PERSONS

Dissertation Submitted for

MD Degree (Branch I) General Medicine

APRIL 2011

The Tamilnadu Dr .M.G.R. Medical University
Chennai – 600 032.

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CERTIFICATE

This is to certify that this dissertation titled "**PREVALENCE OF MICROALBUMINURIA IN NORMOGLYCAEMIC - NORMOTENSIVE OBESE PERSONS" – A CASE CONTROL STUDY** submitted by **DR.M.NATARAJ** to the faculty of General Medicine, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree branch I General Medicine, is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I**, Dr.M.NATARAJ,** solemnly declare that the dissertation titled "**PREVALENCE OF MICROALBUMINURIA IN NORMOGLYCAEMIC - NORMOTENSIVE OBESE PERSONS" - A CASE CONTROL STUDY** has been prepared by me. This is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai,** in partial fulfillment of the regulations for the award of MD degree (Branch I) General Medicine.

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ACKNOWLEDGEMENT

At the outset, I Express my sincere thanks to **THE DEAN,** Madurai Medical College & **Medical Superintendent**, Govt. Rajaji Hospital for permitting me to use the facilities of Madurai Medical College and Government Rajaji Hospital to conduct this study.

I wish to express my respect and sincere gratitude to my beloved teacher and Head of the Department of Medicine, **PROF.DR.MOSES K DANIEL, M.D.,** for his valuable guidance and encouragement throughout the study and also during my post graduate course. I owe my sincere thanks to him.

I also owe my sincere thanks to my unit chief and my guide **PROF.J.SANGUMANI, M.D.,** for his guidance and advice throughout the study.

I express my special thanks to the former Professor & HOD of medicine, **PROF.DR.A.AYYAPPAN.M.D.,** for his valuable guidance. I also owe my special thanks to my former chief & professor **PROF.M.MUTHIAH**. **M.D,** for his guidance in my intial stages of my study .

I am greatly indebted to my beloved teachers, **Dr.S.Vadivelmurugan M.D., Dr.D.D.Venkatraman M.D., Dr.V.T.Premkumar M.D., Dr.M.Natarajan, M.D., Dr.Bagialakshmi M.D, Dr. Dharmaraj M.D,** for their valuable advice throughout my study.

I am extremely thankful to my unit Assistant Professors **Dr.S.Murugesan,M.D**, & **Dr.R.Sundaram,M.D.,** for their valuable support throughout my study and also for making my stay in the unit both informative and pleasurable.

I sincerely thank the staff of the Out patient Department for their cooperation & their support .

I profusely thank the Biochemistry Department for their cooperation and support.

I extend my thanks to my family and friends who have stood by me during my times of need. Their help and support have been invaluable to the study.

Finally, I thank all the patients, who form the most integral part of this study, for their kind cooperation. I pray for their speedy recovery and place this study as a tribute to them.

Above all I thank the Lord Almighty for his kindness and benevolence.

CONTENTS

INTRODUCTION

Obesity has reached epidemic proportions worldwide. Recent World Health Organization (WHO) projections estimate that globally in 2005 approximately 1.6 billion adults older than 15 years were overweight and at least 400 million adults were obese[2] . The WHO also underlines that this pandemic, once considered a problem only in high-income countries, is now dramatically on the rise in low- and middle-income countries (Developing countries), particularly in India & China.

Obesity is now the silent epidemic of this century throughout the world. 26th November of every year is celebrated as " ANTI OBESITY DAY " . In India more than 20 million people are suffering from obesity which should be the root cause of most of the problems in the future.

The studies say that every extra 10kg of weight gain reduces life expectancy by 3yrs. Nowadays the person's life is of hectic lifestyle so they start resort to crash dieting for reducing weight. Crash dieting (measures taken to reduce weight) usually results in loss of body water

and mass, and not fat. There is also a rebound of weight gain, driven by the hormone ghrelin, or the hunger hormone.

Obesity is a disease of energy storage whose etiology is cumulatively greater energy intake than is needed for daily activities. The excess energy is stored in the form of fat, carbohydrate, or protein.

The pathology is, enlarged fat cells. The extent to which these enlarged cells produce detrimental health consequences depends on two major factors.

The first is the mass of fat, which leads to changes in body configuration . The second is the location of the fat cells.

The principal detrimental metabolic consequences occur when fat cells enlarge. Increased intra-abdominal or visceral fat may accentuate this problem.

Production of adipocytokines, inflammatory markers, vascular factors, and leptin from enlarged visceral fat cells causes the primary metabolic derangements, such as diabetes, atherogenic dyslipidemia (decreased HDL cholesterol and increased triglycerides), and release of inflammatory markers such as interleukin 6 (IL-6) and tumor necrosis factor α (TNF-α) or procoagulant factors such as plasminogen activator inhibitor 1 (PAI-1) .

Obesity is a disease and its pathology lies in the increased size and number of fat cells .In adults, the upper limits of the total no of normal fat cells range from 40 x 10^9 to 60 x 10^9. The number of fat cells increases most rapidly during late childhood and puberty.

The number of fat cells can increase three- to fivefold when obesity occurs in childhood or adolescence.

Hypertrophic obesity

Enlarged fat cells is the pathologic sign of obesity[2]. Enlarged fat cells tend to correlate with an android or truncal fat distribution, and are often associated with metabolic disorders such as glucose intolerance, dyslipidemia, hypertension, and coronary artery disease.

These derangements occur because large fat cells secrete more peptides and metabolites, such as IL-6, TNF-α, leptin, and PAI-1. The exception is adiponectin, whose secretion decreases as fat cells enlarge.

Hypercellular obesity

An increase in the number of fat cells usually occurs when obesity develops in childhood. When it begins in early or middle childhood, the type of obesity tends to be more severe. Increased numbers of fat cells may also occur in adult life, and this is to be expected when the body mass index (BMI) is >40 kg/m2.

Measuring fat distribution is important, because increased visceral fat predicts the development of health risks better than the total body fat. The concept that android or male fat distribution was associated with diabetes and heart disease was originally suggested by Vague in 1948 and is now widely accepted.

The distribution of body fat can be estimated by a variety of techniques. The ratio of waist circumference to hip circumference (WHR) was used in the pioneering studies that brought scientific recognition in the 1980s to the relationship of centrally located fat to the risk of developing heart disease, diabetes, and other chronic problems associated with obesity .

More precise estimates of visceral fat can be obtained by computed tomography (CT) or magnetic resonance imaging.

Overweight is now recognized as a risk factor for cardiovascular disease and as a contributing factor in the development of other diseases, most notably diabetes and gall bladder disease. In this context, it is important to evaluate and treat the obesity so as to reduce the overall likelihood for developing disease and to reduce the social consequences of being obese.

Overweight, central or abdominal fat, weight gain after age 20 years, and a sedentary lifestyle all increase health risks and increase economic costs of obesity. Intentional weight loss by overweight individuals, on the other hand, reduces these risks. Although data are not yet available, researchers widely believe that long-term intentional weight loss lowers overall mortality, particularly from diabetes, gallbladder disease, hypertension, heart disease, and some types of cancer.

We know that Visceral adiposity (VAT) is associated with many metabolic risk factors, metabolic syndrome, diabetes, and CVD's. In the clinical setting, measurement of VAT by CT or MRI is not used outside of research protocols[13]. In clinical practice, we can use anthropometric measurements such as WC or WHR to estimate central adiposity.

It has become the sixth most important risk factor contributing to the overall burden of chronic disease worldwide. Obesity is increasingly observed in children. Obesity is closely associated with (although not identical to) metabolic syndrome, which is defined as a cluster of risk factors that increases cardiovascular risk and often is linked to obesity.

Recently, it has been recognized that obesity is not only a cardiovascular risk factor, but also a major risk factor for kidney failure. The final common pathway involves preglomerular vasodilatation with resultant

glomerular hypertrophy and hyperfiltration. This hyperfiltration ultimately results in glomerulosclerosis . This can be detected in the earliest stage itself by measuring microalbuminuria in the urine.

One of the common findings in patients with metabolic syndrome is microalbuminuria. There is ongoing discussion about whether microalbuminuria, in metabolic syndrome, is due to obesity, or due to diabetes, or hypertension.

Whether microalbuminuria in visceral obesity reflects specific glomerular damage or is the marker of generalized endothelial cell dysfunction is still debatable. In view of the known podocyte/endothelial cell interaction, presumably both explanations are true[8].

Weisinger et al provided the first description of focal segmental glomerulosclerosis as a specific renal complication of morbid obesity.This observation has now been confirmed in many studies.

It has been shown that after weight loss, induced by bariatric surgery, markers of kidney damage, including albuminuria and proteinuria, as well as kidney function, have improved in multiple case reports[36].

By the time clinical signs pointing to kidney involvement in obese and metabolic syndrome persons are found, specifically like macroalbuminuria and reduced glomerular filtration rate, the horse has

already left the barn (although there is some recent evidence of reversibility).

It is therefore important to look at the very earliest changes, like measuring microalbuminuria in urine to devise targeted interventions like strategies for weight reduction, drug therapy & surgical methods to reduce weight. Only then will we be able to nip obesity-related kidney disease in the bud.

So with this background in mind , this case control study of 50 selected obese persons with normal blood glucose & blood pressure, & 50 selected nonobese persons with normal blood glucose & blood pressure, attending the outpatient clinic of Govt Rajaji Hospital, Madurai were compared for the prevalence of microalbuminuria, as a marker of endothelial dysfunction & early kidney disease .

This study was undertaken by me in the department of medicine, Govt Rajaji Hospital, Madurai medical college.

It is hoped that this study may help to prevent the development of complications in obese persons , by early detection of microalbuminuria.

This study also stresses the importance of weight reduction & life style modification in obese persons, thereby preventing early morbidity & mortality.

REVIEW OF LITERATURE

2.1.1 Microalbuminuria:

Microalbuminuria is defined as the excretion of 30 to 300mg of albumin per day in urine[1]. It is not a different form or fraction of albumin but just a very small amount of albumin. Albumin molecule is relatively small and it is often the first protein to enter the urine after the kidney is damaged.

	24 hr. Collection (mg / 24 hr)	**Timed collection (µg/min)**	**Spot collection Albumin Creatinine Ratio**	
			µg / mg or mg/g	**mg/mmol**
Normal	< 30	<20	< 30	<3.4
Microalbuminuria	30 – 300	20 – 200	30 – 300	3.4 – 33.9
Macroalbuminuria	>300	>200	>300	>33.9

Excretion of albumin in urine, in the range of 20 to 200µg/min. (30-300mg/day) is called microalbuminuria. This range of albumin in urine cannot be detected by routine urine tests. The presence of increased UAE (Urinary albumin excretion) signals an increase in the transcapillary escape rate of albumin and is therefore a marker of microvascular disease.

During the last few years, a subtle increase in urinary albumin excretion (UAE) not detectable by routine methods, so called microalbuminuria, has been identified as a prognostic marker for renal and/or cardiovascular risk in diabetic and non-diabetic subjects [Hypertension & Obese patients]. Consequently, assessment of microalbuminuria is now recommended as a risk stratification strategy not only in diabetic subjects, but also in hypertensives & obese patients.

Albumin is an electronegative serum protein with a molecular mass of 66,349 Da. After glomerular filtration, part of the albumin is reabsorbed by tubular epithelial cells. Proteases split the albumin molecule into fragments, some of which back-leak into the tubular fluid . In addition, albumin can reach the urine from an inflammatory lesion at any site from the renal pelvis to the urethra. In the absence of inflammation in the urinary tract, intact albumin of glomerular origin is the major source of albumin in the urine and only a small amount of small albumin fragments are present[6].

Albumin can be detected by several methods based on precipitation (boiling, sulphosalicylic acid), dye binding(biuret, tetrabromphenol, albumin blue 580) or immunologic detection (radioimmunoassay, nephelometry, immunoturibidometry). While the immune reactive methods estimate only complete albumin molecules recognized by antibodies, peptide fragments of

albumin can be assessed by dye tests and specific spectrophotometry. The immunologic methods are most frequently used for clinical purposes, not only because they are easy to use at relatively low cost, but also because they are able to detect small amounts of albumin in the urine.

2.1.2 METHODS OF MEASURING MICROALBUMINURIA

Small concentration of albumin in the urine can be measured qualitatively by several methods. Radioimmunoassay was the first and most widely used method. Various methods to determine microalbuminuria are given in the table

Method	**Sensitivity**	**Time of assay**
Single immune radio diffusion	1.25mg/ml	1 day
Electroimmunoassay	5mg/l	4 – 6 hrs
Immunoturibidimetric assay	5mg/l	20 – 30 min
Radio immuno assay	6.2mcg/l	1-2 days
ELISA	250mcg/l	12-18 min
Fluorescent immuno assay	500mcg/l	4-6 hrs
Latex agglutinates immune nephelometry	750mcg/l	6 hrs
Immune chemical semi quantitative dipstick	20-300mg/l	5sec- 5 min

2.1.3 Methods to report UAE

The concentration of urinary albumin depends on the amount of albumin excreted and on the urine concentration. A precise assessment is only possible if these two factors are considered. Methods based on timed urine collection or on simultaneous assessment of urine creatinine concentration have been used to avoid these confounders of the urinary albumin concentration.

Urine albumin concentrations are standardized for concurrent creatinine excretion thus obtaining UACR (urine albumin creatinine ratio). This procedure is based on the concept that creatinine excretion is stable & corrects for unknown urine volumes.

According to ADA the gold standard for measuring urine albumin is a 24hr urine collection. Collecting and measuring albumin in urine samples during 24 h (mg/24 h) or timed-overnight (mg/min) is frequently used in specialized settings.

In contrast, for primary care and epidemiological studies, a correction is performed by simultaneously assessing creatinine excretion (mg/g Cr **or** mg/mmol Cr **or** µg/mg Cr) in spot samples, collected from the first voided urine or at the time of the clinic visit.

Spot urine collection

- **Description**

  Random spot measurement of the albumin-to-creatinine ratio. First void or other morning collections are preferred because of the diurnal variation in albumin excretion

  Albumin and creatinine levels are measured in a single rapid assay

- **Normal**

  <30mcg of albumin/mg creatinine.

- **Abnormal**

  Microalbuminuria: 30-299mcg of albumin/mg creatinine

  Clinical albuminuria: 300mcg or more of albumin/mg creatinine

Timed urine collection

- **Description**

  The amount of albumin excreted over a period of time (e.g. overnight or 4h collection) is measured.

- **Normal**

  <20mcg of albumin/min.

- **Abnormal**

  Microalbuminuria: 20-199mcg of albumin/min

  Clinical albuminuria: 200mcg or more of albumin/min

24-hour urine test

- **Description**

  Urine is collected over a 24-hour period and albumin and creatinine levels measured.

- **Normal**

  <30mg of albumin in 24h.

- **Abnormal**

  Microalbuminuria: 30-299mg of albumin in 24h

  Clinical albuminuria: 300mg or more of albumin in 24h

American diabetes association (ADA) advises that the spot urine collection is often easy to carry out in the O.P setting , and complied by the patient easily than the laborious procedure of collecting 24hrs urine. The first void urine or other morning collections are best because of the diurnal variations in albumin secretion.

2.1.4 Variability of UAE

The variability of UAE is one of the most important limitations of assessment for clinical purposes. It is affected by a large number of factors which must be kept in mind when interpreting the results.

Fever, vigorous exercise, heart failure, haematuria and urinary tract infection produce a transitory increase in UAE which is more or less persistent depending on the cause, the intensity and the duration of the respective condition.

Urinary albumin excretion follows a circadian pattern. In normal volunteers, UAE decreases at nighttime in recumbent position to approximately 70% of the values during the period of activity.

2.1.5 Evaluation of UAE

Conventionally, UAE values have been categorized according to the presence or the absence of microalbuminuria. The presence of microalbuminuria points to a high cardiovascular and/or renal risk which requires intensification of treatment.

Microalbuminuria (MAU) is now considered to be an atherosclerotic risk factor. MAU predicts future cardiovascular disease risk in diabetic patients, in elderly patients, as well as in the general population. It has been implicated as an independent risk factor for cardiovascular disease and premature cardiovascular mortality.

Although microalbuminuria is associated with a certain degree of sub-clinical artherosclerotic damage, it is not known how early in the atherosclerotic process microalbuminuria appears.

Epidemiological studies have shown an association between MAU and insulin resistance, obesity, salt sensitivity and dyslipidaemia in patients with essential hypertension and diabetes. The mechanisms linking microalbuminuria and risk for cardiovascular disease are not fully understood, but in subjects at risk it may be related to increased transvascular leakiness of albumin in systemic as well as renal vessels.

A recent concept is that microalbuminuria is a marker of extensive endothelial dysfunction or generalised vasculopathy, which may lead to heightened atherogenic states. One possible explanation is that endothelial dysfunction might promote increased penetration of atherogenic lipoprotein particles in the arterial wall, but glycaemic status, insulin resistance, procoagulant state and adhesion molecules have all been implicated in the pathogenesis.

Current evidence suggests that inhibitors of the renin-angiotensin system (RAS) can prevent or delay the progression of microalbuminuria to

overt nephropathy in normotensive persons. Whether albuminuria is a risk factor or just a marker for CV disease, it identifies the high-risk patients who should be targeted for early, aggressive interventions against proven risk factors.

If persistent microalbuminuria is confirmed, strict blood pressure control with added RAS inhibition should be pursued in an attempt to stabilise or even reduce microalbuminuria, preserve kidney function and possibly improve cardiovascular risk.

The greater the reduction of UAE, the lower the cardiovascular risk. Monitoring UAE can therefore be clinically useful to assess the success of interventions.

Risk factors associated with microalbuminuria:

Non modifiable	**Modifiable**	
	Well documented	**Likely**
Race/ethnicity	Diabetes	Hyperlipidemia
Male gender	Hypertension	High salt diet
Older age	Obesity	Oral contraceptives
Low birth weight	Smoking	Hormone replacement therapy

2.1.6 PATHOPHYSIOLOGY OF MICROALBUMINURIA

Glomerular & tubular mechanisms

The intimate relationship between low level albumin excretion & vascular permeability makes urinary albumin excretion , highly sensitive to the presence of any inflammatory process, including cardiovascular disease. The kidney is ideally placed to amplify any small changes in systemic vascular permeability .

The glomeruli receive 25% of the cardiac output. Of the 70kg of albumin that pass through the kidneys every 24 hr, less than 0.01% reaches the glomerular ultrafiltrate (i.e, less than 7g/24 hr) and hence enters the renal tubules.

Almost all filtered albumin is reabsorbed by the proximal tubule via a high – affinity, low – capacity endocytotic mechanism, with only 10-30mg/24hr appearing in the urine. Assuming that , 7g of albumin is filtered every 24 hr, a 1% increase in systemic vascular permeability in response to an inflammatory stimulus would result in an additional 70mg of albumin into the filtrate. Since tubular mechanisms for albumin reabsorption are near saturation, urinary albumin excretion would increase from a maximum of 30 to approximately 100mg/24 hr.

Glomerular permeability to albumin is dependant on endothelial charge selectivity as well as size selectivity. The negative charge conferred on the glomerular membrane by its constituent glycoproteins plays a role in restricting the permeability of glomerular charge selectivity, and this is found in both diabetic & non diabetic populations with microalbuminuria.

2.1.7 **Proteins in normal urine**

Charge and size selectivity normally prevent virtually all plasma albumin, globulins & other large molecular weight proteins from crossing the glomerular wall. However , if this barrier is disrupted, there can be leakage of plasma proteins into the urine. Smaller proteins < 20kda are freely filtered but are readily reabsorbed by the proximal tubule.

Normal individuals excrete < 150 mg/ day of total protein & < 30 mg/day of albumin. The remainder of the protein in the urine is secreted by the tubules, (Tamm-Horsfall protein, IgA , & Urokinase) and represents small amounts of filtered β2- microglobulin, apoproteins, enzymes, & peptide hormones.

ACE inhibitors & ARB's in particular are associated with renoprotection. They can be given in this stage of microalbuminuria to

prevent its progression to macroalbuminuria. These effects are mediated by reducing intraglomerular pressure and by inhibition of angiotensin driven sclerosing pathways, in part through inhibition of TGF-β mediated pathways.

2.1.8 Factors that cluster with microalbuminuria

Microalbuminuria may be related to target organ damage by several biological pathways:

1) Insulin resistance
2) Central obesity
3) Low levels of high-density lipoprotein
4) High triglyceride levels
5) Systolic hypertension
6) Lack of nocturnal dip in B.P on 24 hr monitoring
7) Salt sensitivity
8) Endothelial dysfunction
9) Hypercoagulability
10) Impaired fibrinolysis
11) Renal dysfunction

2.1.9 Interventions to reduce microalbuminuria

Endothelial dysfunction occurs early in patients with microalbuminuria. Several large studies have shown that modulating microalbuminuria has beneficial effects.

***Non pharmacological measures**:*

These include weight loss, exercise, and eating a low fat diet, but most of the time these are not enough.

Pharmacological agents:

Statins, ACE inhibitors, & ARB's have been shown in several land mark studies to decrease high blood pressure and microalbuminuria.

Either ACEI or ARB's should be used to reduce the progression from microalbuminuria to macroalbuminuria & the associated decline in GFR. After 2-3 months of therapy , the drug dose is increased until either the microalbuminuria disappears or the maximum drug dose is reached.

But once macroalbuminuria ensues , the likelihood of ESRD is high.

2.2.1 Obesity

Obesity results from the complex interaction of environmental factors that act on a genetic background that determines the susceptibility to obesity. Obesity results from an imbalance of energy expenditure and energy intake. over the last two decades, it has become clear that genetic factors play an important role in the determination of body weight[2].

Current definitions of obesity are based on the ratio of bodyweight (in kg) and height squared (in m2) and expressed as body mass index (BMI) with a normal BMI defined as 20–24.9, moderate overweight between 25–29.9 and Gr I obesity as above 30 and Gr II obesity > 35 and morbid obesity as > 40. In 2000, the World Health Organisation released the following statement: 'Obesity is a chronic disease, prevalent in both developed and developing countries, and affecting children as well as adults[2,5].

Obesity is a leading preventable cause of death worldwide, with increasing prevalence in both children & adults. It is defined by body mass index (BMI) and further evaluated in terms of fat distribution via the waist–hip ratio . BMI is closely related to both percentage body fat and total body fat[2].

BMI	CLASSIFICATION
<18.5	Underweight
18.5 – 24.9	Normal Weight
25 – 29.9	Overweight
30 – 34.9	Class I Obesity
35 – 39.9	Class II Obesity
>= 40	Class III Obesity

2.2.2 Effects on health

Excessive body weight is associated with various diseases, particularly cardiovascular diseases, diabetes mellitus type 2, obstructive sleep apnea, certain types of cancer, and osteoarthritis. As a result, obesity has been found to reduce life expectancy.

Morbidity

Obesity increases the risk of many physical and mental conditions. These comorbidities are most commonly shown in metabolic syndrome , a combination of medical disorders which includes: diabetes mellitus type 2,

high blood pressure, high total blood cholesterol, and high triglyceride levels.

Complications are either directly caused by obesity or indirectly related through mechanisms sharing a common cause such as a poor diet or a sedentary lifestyle.

Health consequences fall into two broad categories:

1) Those attributable to the effects of increased fat mass (such as osteoarthritis, obstructive sleep apnea, social stigmatization)
2) Those due to the increased number of fat cells (diabetes, cancer, cardiovascular disease , non-alcoholic fatty liver disease)

Increases in body fat alter the body's response to insulin, potentially leading to insulin resistance. Increased fat also creates a proinflammatory state, and a prothrombotic state.

2.2.3 Abdominal obesity

Visceral fat or **abdominal fat** , also known as organ fat or **intra-abdominal fat**, is located inside the abdominal cavity, packed in between organs (stomach, liver, intestines, kidneys, etc.). Visceral fat is different

from subcutaneous fat underneath the skin, and intramuscular fat interspersed in skeletal muscles.

Fat in the lower body, as in thighs and buttocks, is subcutaneous, whereas fat in the abdomen is mostly visceral. Visceral fat is composed of several adipose depots including mesenteric, epididymal white adipose tissue (EWAT) and perirenal depots.

An excess of visceral fat is known as central obesity, or "belly fat", in which the abdomen protrudes excessively. There is a strong correlation between central obesity and cardiovascular disease. Excess visceral fat is also linked to diabetes, insulin resistance, inflammatory diseases, and other obesity-related diseases.

Female sex hormone causes fat to be stored in the buttocks, thighs, and hips in women. Men are more likely to have fat stored in the belly due to sex hormone differences. When women reach menopause and the estrogen produced by ovaries declines, fat migrates from their buttocks, hips and thighs to their waists, later fat is stored in the belly.

Abdominal fat has a different metabolic profile—being more prone to induce insulin resistance. This explains to a large degree why central

obesity is a marker of impaired glucose tolerance and is an independent risk factor for cardiovascular disease (even in the absence of diabetes mellitus and hypertension).

Adipose tissue derived hormones include[12]:

- Adiponectin
- Leptin
- Plasminogen activator inhibitor-1 (PAI-1)
- TNFα
- IL-6
- Resistin
- Estradiol (E2)

Adipose tissue is the greatest peripheral source of aromatase in both males and females contributing to the production of estradiol

Adipose tissues also secrete a type of cytokines (cell-to-cell signalling proteins) called adipokines (adipocytokines) which play a role in obesity-associated complications.

Body fat meter

A **body fat meter** is a widely available tool used to measure the percentage of fat in the human body. Different meters use various methods to determine the body fat to weight ratio.

The body fat meter uses the principle of bioelectrical impedance analysis (BIA) to determine an individual's body fat percentage.

2.2.4 Waist-hip ratio & waist circumference[13]

Waist-hip ratio or **Waist-to-hip ratio** (**WHR**) is the ratio of the circumference of the waist to that of the hips. It is calculated by measuring the smaller circumference of the natural waist (WC), usually just above the belly button, and dividing by the hip circumference at its widest part of the buttocks or hip. The ratio is applied both to women and men. Men generally have much less pronounced hips, relative to waist size. The acceptable waist circumference in men $\leq$ 102 cm & in women $\leq$ 88 cm.

The WHR has been used as an indicator or measure of the health of a person, and the risk of developing serious health conditions. Research shows that people with "apple-shaped" bodies (with more weight around the waist)

face more health risks than those with "pear-shaped" bodies who carry more weight around the hips.

WHR is used as a measurement of obesity, which in turn is a possible indicator of other more serious health conditions.

A WHR of 0.8 for women and 0.9 for men have been shown to correlate strongly with general health and fertility. Women within the 0.8 range have optimal levels of estrogen and are less susceptible to major diseases such as diabetes, cardiovascular disorders and ovarian cancers. Men with WHRs around 0.9, similarly, have been shown to be more healthy and fertile with less prostate cancer and testicular cancer.

WHR has been found to be a more efficient predictor of mortality in older people than waist circumference or body mass index (BMI). If obesity is redefined using WHR instead of BMI, the proportion of people categorized as at risk of heart attack worldwide increases threefold.

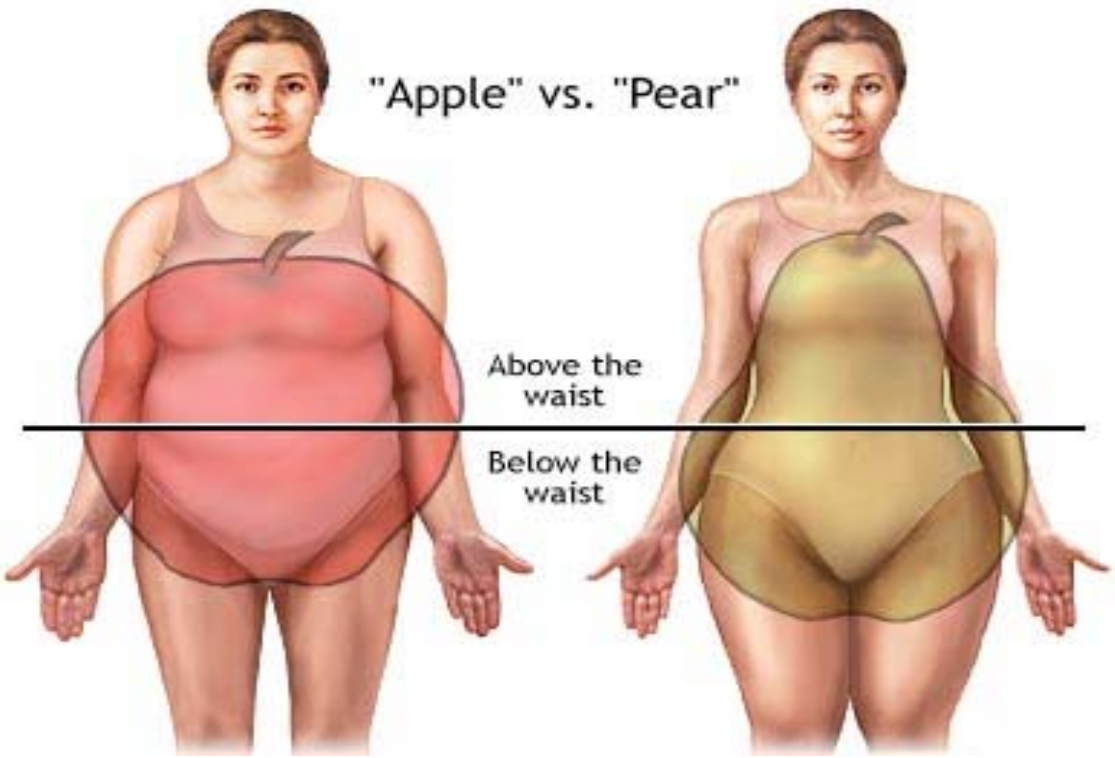
The body fat percentage is considered to be an even more accurate measure of relative weight. Of these three measurements, only the waist-hip ratio takes account of the differences in body structure. Hence, it is possible for two women to have vastly different body mass indices but the same

waist-hip ratio, or to have the same body mass index but vastly different waist-hip ratios.

	BMI (kg/m^2)	**Obesity Class**	**Men ≤102 cm Women ≤88 cm**	**Men >102 cm Women >88 cm**
			Waist circumference	
Underweight	18.5		-----	-----
Normal+	18.5 - 24.9		-----	-----
Overweight	25.0 - 29.9		Increased	High
Obesity	30.0 - 34.9	I	High	Very High
	35.0 - 39.9	II	Very High	Very High
Extreme Obesity	≥40	III	Extremely High	Extremely High

Waist – Hip Ratio:

	Acceptable		Unacceptable		
	excellent	**good**	**average**	**high**	**extreme**
Male	< 0.85	0.85 - 0.90	0.90 - 0.95	0.95 - 1.00	> 1.00
Female	< 0.75	0.75 - 0.80	0.80 - 0.85	0.85 - 0.90	> 0.90



2.2.5 Obesity & Renal Disease

Obesity is a recognised risk factor for the development of nephropathy, especially focal segmental glomerulosclerosis (FSGS).

The structural changes occurring in human kidney as a consequence of obesity have been demonstrated in large retrospective studies.

The obesity associated FSGS differs from idiopathic FSGS in many ways. Distinct clinicopathological features such as glomerulomegaly, less severe, foot process effacement and the absence of features of the nephrotic syndrome despite nephrotic range proteinuria are helpful in differentiating this entity from the idiopathic FSGS. Obesity associated FSGS is an indicator of poor prognosis with nearly 50% developing advanced renal failure.

Glomerular hyperfiltration/hypertrophy in response to the increased metabolic needs of obesity are postulated to lead to the development of glomerulosclerosis (GS) in a manner analogous to that in reduced renal mass states. Nevertheless, the individual risk for developing GS with obesity is very low.

It is proposed that glomerular hyperfiltration/hypertrophy per se are not pathogenic, in the absence of an enhanced glomerular blood pressure (BP) transmission. The modest preglomerular vasodilation that is likely to be

present in the large majority of obese individuals is not sufficient to result in such increased BP transmission.

However, in the small subset of obese individuals who are also born with a substantially reduced nephron number, there is a greater risk of enhanced glomerular BP transmission due to the substantially greater preglomerular vasodilation. Perhaps this is of greater clinical importance, (i.e.,) similar additive deleterious effects of obesity on glomerular BP transmission would be expected in individuals with reduced renal mass, either congenital or acquired, or with concurrent renal disease, leading to accelerated progression.

Obesity is associated with the activation of RAS, increased sympathetic nervous system activity, and hyperinsulinaemia, all of which may contribute to sodium reabsorption. A compensatory lowered renal vascular resistance, elevated kidney plasma flow, increased GFR, and the higher blood pressure associated with obesity are important in overcoming the increased sodium reabsorption.

Neurohumoral factors, like angiotensin II, the sympathetic system and cytokines, impaired pressure natriuresis, are the adaptive changes leading to increased glomerular wall stress. These adaptive changes in the presence of other risk factors, e.g., hyperlipidaemia and hyperglycaemia, may provoke

glomerulosclerosis, proteinuria, and loss of nephron function in the 'obese kidney', even before structural changes are evident. The combination of these potentially nephrotoxic mechanisms, including hyperfiltration and hypertension may initiate and perpetuate renal damage.

Persistent obesity causes renal injury and functional nephron loss, contributing to elevated blood pressure, which in turn leads to further renal injury, thereby setting off a vicious cycle of events leading to further elevated blood pressure and renal injury.

Obesity certainly is better prevented than treated. Thus, lifestyle and dietary modifications should be encouraged in the society to control the obesity pandemic and reduce the burden of obesity-related health hazards. Weight reduction early in the course and the use of ACE inhibitors and statins might improve the outcome of obesity-related renal disorders.

2.2.6 Obesity & Microalbuminuria

Obesity has been reported to be an independent risk factor for the development of proteinuria. In nonhypertensive subjects, the prevalence of microalbuminuria is positively correlated with the increase in BMI and increase in waist-to-hip ratios. Signs of early endothelial dysfunction manifested as microalbuminuria were strongly and independently associated with central obesity.

Mechanisms of obesity inducing proteinuria and Glomerulosclerosis are :

a. Glomerular hyperfiltration

An increased renal blood flow and GFR, mediated by vasodilatation of afferent arterioles has been observed in obese persons[31].

The cause of these haemodynamic changes could be related to an increased salt reabsorption in the loop of Henle and thus increased GFR through tubuloglomerular feedback. The mechanisms for increased tubular reabsorption are still unclear, but experimental studies have shown that consistently found disturbances in obesity, i.e., insulin resistance, increased sympathetic activity and activated reninangiotensin system (RAS), could all play an important role.

b. Hyperlipidaemia

Obesity is commonly associated with hyperlipidemia. Studies have shown hyperlipidaemia to cause mesangial proliferation and expansion due to LDL cholesterol and development of glomerulosclerosis and progressive renal failure. Treatment of Hyperlipidaemia reduces glomerular injury in obese persons.

c. Role of leptin and other adipose-derived hormones:[8,11,16]

Leptin is encoded on the 'ob' gene and is a peptide hormone derived from adipose tissue and plays a critical role in the control of appetite and energy expenditure. Leptin has been shown to promote the development of proteinuria and FSGS. Additional direct or indirect effects of leptin on the kidney include natriuresis, angiotensin-2 production, increased sympathetic nervous activity, and stimulation of reactive oxygen species. As mainly the kidneys clear leptin, increased levels of leptin in chronic renal failure contribute to appetite suppression.

Adiponectin is a secretory protein expressed in adipocytes. Normal level in serum is 5 – 30 µg/ml. It is a potent insulin enhancer, it decreases insulin resistance. Adiponectin, an anti-inflammatory cytokine, is a product of adipose tissue and is involved in regulation of lipid and glucose metabolism.

Adiponectin attenuates the endothelial inflammatory response by inhibiting the endothelial expression of vascular cell and intercellular adhesion molecules (VCAM-1 and ICAM-1) and Eselectin which are triggered by inflammatory cytokines.

Adiponectin primarily regulates albuminuria through its alteration of podocyte function. It acts through AMPK pathway .Plasma

concentrations of adiponectin are low in visceral obesity & this produces fusion of podocyte foot processes – leads to increased albuminuria. These suggest that higher adiponectin levels confer a protective effect against atherosclerosis.

Manoevures that can increase adiponectin levels are

1) Weight reduction
2) RAS blockade
3) PPAR γ agonists
4) Metformin –increases AMPK(5'c-AMP activated protein kinase) pathway – the pathway to modulate oxidant stress in podocytes.

Angiotensinogen and angiotensin II are expressed in human adipose tissue and these play an important role in the genesis of obesity-related hypertension and subsequent glomerular injury.

Tumour necrosis factor-α is involved in insulin resistance and inflammation and adipose tissue is a significant site for its synthesis. *TNF-α* is recognised as a mediator of glomerulosclerosis and is produced by adipocytes5.

Plasminogen activator inhibitor is a procoagulative agent that inhibits fibrinolysis and is synthesised in abundance in the adipose tissue and plays an important role in vascular injury and atherosclerosis.

2.2.7 Obesity & Structural changes in the kidney:[39,40]

The changes in the kidney includes expansion of Bowman's capsule, cell proliferation in the glomeruli, thickening of glomerular and tubular basement membranes and increased mesangial matrix in many glomeruli, and increases in TGF-ß1 expression in the cortex.

These histologic changes were associated with marked glomerular hyperfiltration and increased renal plasma flow, modest increases in arterial BP, increased plasma renin activity, and hyperinsulinemia.

In addition to the hemodynamic alterations, there are also hormonal changes that could contribute to renal remodelling in obesity. Two possibilities include elevated plasma Ang-II levels and hyperinsulinemia, both of which occur in obesity. Evidence that elevated plasma AngII and insulin levels may contribute to glomerular structural changes is derived primarily from *in vitro* studies of mesangial cell cultures.

Moreover TGF-ß1 has been suggested to promote renal structural changes and fibrosis in several kidney disorders, including diabetic nephropathy and obesity.

2.3 Metabolic syndrome

Metabolic syndrome is a combination of medical disorders that increase the risk of developing cardiovascular disease. Metabolic syndrome is also known as metabolic syndrome X**,** syndrome X**,** insulin resistance syndrome**.**

The World Health Organization criteria requires the presence of

1) Diabetes mellitus, or impaired glucose tolerance, or impaired fasting glucose or insulin resistance, AND any two of the following:

a) Blood pressure: ≥ 140/90 mmHg

b) Dyslipidemia: triglycerides (TGL) ≥ 150 mg/dl and high-density lipoprotein cholesterol (HDL-C) <35 mg/dl (male), or < 40 mg/dl (female)

c) Central obesity: waist:hip ratio > 0.90 (male); > 0.85 (female), or body mass index > 30 kg/m^2

d) Microalbuminuria: urinary albumin excretion ratio ≥ 20 μg/min or albumin:creatinine ratio ≥ 30 mg/g

Associated diseases and signs are: hyperuricemia, fatty liver (especially in concurrent obesity) progressing to non-alcoholic fatty liver disease, polycystic ovarian syndrome (in women), and acanthosis nigricans.

2.4 Studies relating Obesity & Microalbuminuria:

1) Jackson Heart Study: - it deals with prevalence of microalbuminuria in obese non-diabetic, normotensive African Americans. It states that obesity per se is a major risk factor for renal disease even in the absence of diabetes.

Summerso et al reported that the prevalence of microalbuminuria in obese individuals at 31.6% when compared to normal individuals.

2) Another study by Eyup Koc, Murat Suher, Gulden Bayrak in Ankara, Turkey , was done on the " Effects of Anthropometric Measurements on Renal function" – it showed the prevalence of microalbuminuria to be 27.3% in persons with increased BMI, & 21.1% in persons with increased WC, & 29.2% in persons with increased WHR.

3) A large scale trial of Australian adults was carried out by Robert C. Atkins, Kevan R, Steven J. Chadban, Ester M for prevalence of microalbuminuria & for its associations. It concluded by saying that

microalbuminuria is associated with Hypertension in 64% of adults , 20.7% of smoking adults, 13.5% of obese adults.

4) A study done by Christine M Hoehner, Kurt J Greenlund, Michelle L. Casper in Atlanta , USA, said that the prevalence of microalbuminuria in nondiabetic native Americans , was 15.2% in relation to other traits of Metabolic syndrome.

5) The insulin resistance atherosclerosis study done by Leena Mykannen, Daniel J.Zaccaro, David C.Robbins, in Texas , USA, has shown that microalbuminuria is associated with Insulin resistance in non-diabetic obese subjects.

6) An article by J S Sandhu, M Singla, A Ahuja, P Chopra from Ludhiana, Punjab have dealt in detail about the renal risks of Obesity. It quotes an increased prevalence of microalbuminuria among obese individuals.

7) Another study by Prataap K. Chandie shaw, Stefan P. Bergar, Marko Mallat, Ton J Rabelink, from The Hague , Netherlands, have shown that central Obesity is an independant risk factor for albuminuria in non-diabetic south asian subjects. In this study they have explored the

hypothesis that central obesity is associated with development of renal injury, prior to the manifestation of diabetes or hypertension.

There are many studies under trial to prove the link between Obesity & its attendant renal & CV risks , by way of identifying the prevalence of microalbuminuria in Obese persons, so that early interventions could be carried out to halt the progression of renal disease & its impact on Cardiovascular system.

AIMS & OBJECTIVES

1) To study the prevalence of microalbuminuria in normoglycaemic-normotensive obese persons (cases) in comparison with nonobese persons (controls).

2) To study the strength of correlation between microalbuminuria & and various grades of obesity in relation to body mass index (BMI) among the cases.

3) To study the strength of correlation between microalbuminuria & waist hip ratio (WHR) in both males and females among the cases.

4) To study the strength of correlation between microalbuminuria & waist circumference (WC) in both males and females among the cases.

MATERIALS & METHODS

SETTING:

This study was done on the subjects attending for their ailments to the out patient clinic of Govt Rajaji Hospital, Madurai.

DESIGN OF STUDY:

A Case – Control study.

PERIOD OF THE STUDY:

Over Eight Months Period (March-2010 -October-2010)

SAMPLE SIZE & SELECTION OF STUDY SUBJECTS:

Persons who attended the outpatient clinic of Govt Rajaji Hospital for some other complaints, & who were obese, over the above eight months period were screened to rule out hypertension , hyperglycemia, macroalbuminuria , dyslipidemia & after ruling out these conditions about 50 obese persons (cases) were included along with 50 nonobese persons (controls) in this study from the above same period.

DETAILS OF STUDY SUBJECTS:

The obese & nonobese persons coming to the out patient department for some other complaints were screened for

1) Blood pressure- was recorded using sphygmomanometer with standard cuff on two occasions 10 minutes apart. Patient should have refrained from smoking for atleast 30 minutes before measuring B.P. , & he should be calm.

2)Persons height & weight was measured in the O.P, and the patient's BMI was calculated using the formula Weight / Height^2.

3)Persons waist circumference, hip circumference was measured with an inch tape & Waist-Hip ratio was calculated.

4)All had undergone lab investigations for

a) Random blood sugar, serum urea, creatinine & Total cholesterol was estimated by an AutoAnalyzer.

b) all the persons had routine urine analysis (albumin by dipstick method, sugar & deposits) done.

c) A 12 lead electrocardiogram was taken.

5) Finally after ruling out hypertension, hyperglycemia, dyslipidemia, & macroalbuminuria about 50 obese persons & 50 nonobese persons underwent urine test for microalbuminuria .

Among the 50 obese persons 26 were males, & 24 were females.

PROCEDURE OF MICROALBUMINURIA TEST:

All the obese & nonobese persons selected by the above method were asked to report the next day morning with first voided early morning urine sample for the detection of microalbuminuria.

It is a fully automated calibrated system. **Urine Albumin to Creatinine ratio** in the given sample was calculated.

Albumin

- Technology - fully automated immunoturbidimetric assay
- Method – photometry
- Reference - adults range <18µg/ml

Creatinine

- Technology –Modified JAFFE method
- Method – Photometry
- Reference range a) Males – 39-259 mg/dl

b) Females – 28-217 mg/dl

EXCLUSION CRITERIA (for cases & controls)

- Persons with RBS (Random Blood Sugar) >140mg/dl (Hyperglycemia)
- Persons with B.P >120/80mm of hg (Hypertension & prehypertension)
- Persons with Total cholesterol > 200mg/dl (Dyslipidemia)
- Persons with urea >40mg/dl & Creatinine > 1.2mg/dl
- Persons with Macroalbuminuria positive (Dip stick method)
- Persons having ischemic changes in ECG.
- Elderly persons >60 yrs
- Persons who are chronic Smokers

Persons with BMI <25 were taken as controls, ≥25 as cases.

ETHICAL COMMITTEE APPROVAL:

Ethical committee clearance was obtained.

CONSENT:

Informed consent were obtained from all the subjects (cases & controls).

STATISTICAL ANALYSIS:

Computer analysis of the collected data was done using the software, **SPSS Statistics Software Version 17.0**. The Pearson Chi-Square Test was used for testing the significance of the collected data.

RESULTS AND ANALYSIS

Table No 5.1:

MEASURES OF CENTRAL TENDENCIES AMONG VARIOUS VARIABLES IN THE STUDY GROUP.

		Age	Ht	Wt	WC	HC
Cases	**Valid**	50	50	50	50	50
	Missing	0	0	0	0	0
Mean		37.96	165.14	81.72	95.52	97.38
Median		39.50	166.00	80.00	95.00	98.00
Mode		48	160	80	90	96
Std. Deviation		8.978	5.249	8.531	7.579	4.911
Range		38	24	34	31	20
Minimum		16	154	64	81	88
Maximum		54	178	98	112	108

This table shows the various variables present in the study group like age, height, weight, waist circumference, & hip circumference and its measure of central tendency & dispersion including the maximum & minimum of all the variables.

Table No 5.2:

Comparison of prevalence of microalbuminuria among both cases & controls.

Microalbuminuria among cases & controls

			MAU		Total
			Normal	**Micro**	
Category	Case	Count	34	16	50
		% within Category	68.0%	32.0%	
	Control	Count	48	2	50
		% within Category	96.0%	4.0%	
Total		Count	82	18	100
		% within Category	82.0%	18.0%	

Table No 5.3:

Chi-Square Test

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi- Square	13.279[a]	1	.000

In this study there were a total of 50 cases (obese persons) ,& 50 controls (non obese persons) , who were screened for microalbuminuria. Out of the 50 cases 16 persons tested positive for microalbuminuria, and out of the 50 controls only 2 persons tested for microalbuminuria. Hence among the obese group who had normal B.P & normal Blood sugar , 16 had microalbuminuria. But in the control group who also had normal B.P & normal blood sugar , only 2 tested positive for microalbuminuria.

After statistical analysis of these values , according to Chi-square test the p value is <0.001 , which is statistically significant, & hence it shows that obesity itself can lead to microalbuminuria & that there is strong correlation between Obesity & Microalbuminuria.

Table No 5.4:

Prevalence of microalbuminuria among various grades of obesity cases based on BMI

Category				Microalbuminuria		Total
				Normal	Micro	
Case	BMI	Overweight	Count	26	3	29
			% within BMI	89.7%	10.3%	
		Obe_Grade1	Count	8	10	18
			% within BMI	44.4%	55.6%	
		Obe_Grade2	Count	0	3	3
			% within BMI	.0%	100.0%	
	Total		Count	34	16	50
			% within BMI	68.0%	32.0%	

Here the persons in the cases list were divided into 3 categories based on the BMI value, into overweight , obesity grade 1, & obesity grade 2. The prevalence of microalbuminuria among all these categories were tabulated and the significance assessed. There was no obesity GR III persons in this study.

Table No 5.5:

Chi-Square Tests				
Category		**Value**	**df**	**Asymp. Sig. (2-sided)**
Case	Pearson Chi-Square	17.215[a]	2	.000
	Likelihood Ratio	18.666	2	.000
	Linear-by-Linear Association	16.870	1	.000
	No of Valid Cases	50		

After the statistical analysis , the Chi-Square test gives the p value as <0.001 , which is statistically very significant.

This goes on to show that there is increasing percentage of the cases with microalbuminuria, with increase in grades of Obesity according to BMI.

Hence there is a strong correlation between BMI & Microalbuminuria. Among the overweight category of 29 persons 3 had microalbuminuria, among 18 grade 1 obesity persons 10 had microalbuminuria, & among 3 grade 2 obesity persons all had microalbuminuria.

So from this study there is a significant relation between BMI & microalbuminuria.

Table No 5.6:

Prevalence of microalbuminuria among male cases based on WHR

WHR & MAU - Males:				Microalbuminuria		
				Normal	Micro	Total
Male	WHR	Acceptable	Count	2	0	2
			% within WHR	100.0%	.0%	
		Unacceptable	Count	17	7	24
			% within WHR	70.8%	29.2%	
	Total		Count	19	7	26
			% within WHR	73.1%	26.9%	

Here the acceptable WHR for males is taken as <0.90 & and the rest of the values as unacceptable WHR .

Most of the males (24 out of 26) from this study come under the category of unacceptable WHR. Only 2 of them come under the acceptable category, & among the 2 none had MAU.

But out of 24 unacceptable , 7 of them had MAU i.e 29.2% had microalbuminuria. Whether this value is significant or not , was derived from the Chi- Square test.

Table No 5.7:

Chi Square Test

Male	Pearson Chi-Square	.798	1	.372

The Chi-Square test was done & the p value was >0.05, hence it was not statistically significant. Hence the relation between WHR & microalbuminuria is by mere chance only, from this study.

So from this study there was no significant correlation between WHR & microalbuminuria for male cases. But since most of them were in the unacceptable category , we could not exactly say whether WHR has a correlation with microalbuminuria or not. Here in the study all the positive microalbuminurics were only from the unacceptable WHR category.

To find out the strength of correlation between WHR & MAU , there should be more no of acceptable category of WHR cases also in the study & the study sample should also be more, then only the exact significance could be arrived at.

Though the prevalence of microalbuminuria among unacceptable male cases based on waist hip ratio was high, it was statistically not significant.

Table No 5.8:

Prevalence of microalbuminuria among female cases based on WHR

WHR & MAU - Females:				Microalbuminuria		Total
				Normal	Micro	
Female	WHR	Acceptable	Count	3	0	3
			% within WHR	100.0%	.0%	
		Unacceptable	Count	12	9	21
			% within WHR	57.1%	42.9%	
	Total		Count	15	9	24
			% within WHR	62.5%	37.5%	

Here out of a total of 24 female cases , 21 females were in the unacceptable WHR category (> 0.80) & 3 of them were in the acceptable WHR category (<0.80).

Among the acceptable category none had microalbuminuria, but among the unacceptable category 9 of them had microalbuminuria.

So we go on to find out the statistical significance based on the Chi-Square test.

Table No 5.9: Chi-Square Tests

Sex		Value	df	Asymp. Sig. (2-sided)
Female	Pearson Chi-Square	2.057[a]	1	.151

So from the above chi-square test , the p value is >0.05, hence the correlation between WHR & microalbuminuria in female cases is statistically not significant.

Hence the increased prevalence of MAU in female cases among the unacceptable WHR category is by chance only. There is no significant correlation between them.

Table No 5.10:

Prevalence of microalbuminuria among male cases based on WC.

WC & MAU - Males				Microalbuminuria		Total
				Normal	Micro	
Male	WC	Acceptable	Count	18	2	20
			% within WC	90.0%	10.0%	
		Unacceptable	Count	1	5	6
			% within WC	16.7%	83.3%	
	Total		Count	19	7	26
			% within WC	73.1%	26.9%	

Table No 5.11:

Chi-Square Test.

Sex		Value	df	Asymp. Sig. (2-sided)
Male	Pearson Chi-Square	12.616[c]	1	.000

The acceptable WC in males is taken as 102 cms. Above this value it is taken as unacceptable.

Going on to compare the prevalence of microalbuminuria among them, we have 20 male cases within the acceptable category & 2 among them have microalbuminuria.

A total of 6 male cases were among the unacceptable category of WC , & among them 5 had microalbuminuria.

The statistical significance was calculated by the Chi-Square Test. The p value was < 0.001 , hence it was very significant.

Hence from this study there was significant correlation between WC & microalbuminuria among the male cases.

So male cases with unacceptable WC had more prevalence of microalbuminuria than with acceptable WC.

Table No 5.12:

Prevalence of microalbuminuria among female cases based on WC.

WC & MAU -Females

Sex				Microalbuminuria		Total
				Normal	Micro	
Female	WC	Acceptable	Count	5	2	7
			% within WC	71.4%	28.6%	
		Unacceptable	Count	10	7	17
			% within WC	58.8%	41.2%	
	Total		Count	15	9	24
			% within WC	62.5%	37.5%	

Table No 5.13:

Chi-Square Test

Sex		Value	df	Asymp. Sig. (2-sided)
Female	Pearson Chi-Square	.336[a]	1	.562

The acceptable WC value for females is taken as <88 cms. Above this it is taken as unacceptable.

Out of a total of 24 female cases 17 were in the unacceptable range & the rest of 7 cases were in the acceptable range.

Among the acceptable cases 2 of them had microalbuminuria & among the unacceptable cases 7 had microalbuminuria.

The statistical significance based on the chi-square test was calculated. The p value was >0.05, hence this correlation was not significant.

Hence from this study it shows that there is no significant correlation between the prevalence of microalbuminuria & WC among the female cases.

Through the prevalence of microalbuminuria among unacceptable female cases based on waist circumference was high, it was statistically not significant.

DISCUSSION

In the present study , there were 50 persons who were obese, & 50 controls who were Non-obese . They were selected based on BMI with value ≥ 25 as obese & <25 as non-obese.

All the persons had normal B.P & normal blood sugar. All had total cholesterol < 200 mg/dl. All had their urea & creatinine within normal range. Their ECG was normal. Their urine was Negative for macroalbuminuria by dipstick method.

They had their height, weight, WC , & hip circumference measured. From these values BMI & WHR was calculated. Then all the cases & controls had their urine checked for microalbuminuria to find out its prevalence.

Among the 50 obese cases 16 had microalbuminuria & among the 50 non obese controls only 2 had microalbuminuria. So on comparing the prevalence of microalbuminuria among cases & controls, according to chi-square test , the p value was <0.001, which was highly significant.

So persons who were obese had significantly high microalbuminuria prevalence (32%). It was comparable to the jackson

heart study among the African Americans , in which the prevalence of microalbuminuria among obese was 31.6%.

BMI & MAU

Next among the cases we studied the severity of correlation of microalbuminuria with grades of obesity based on BMI. The BMI based classification of obesity is common to both males & females. So based on the BMI the cases were separated into overweight , grade I obesity, grade II obesity categories.

Then we studied the prevalence of microalbuminuria among the three categories. Among 29 overweight cases only 3 had microalbuminuria, among 18 grade I obesity cases 10 of them had microalbuminuria, & among 3 grade II obesity cases all of them had microalbuminuria. In this study nobody was in grade III obesity range.

This signifies that as BMI increases the prevalence of microalbuminuria also increases. The p value for this association was <0.001 & it was stastistically highly significant.

The inference is that the prevalence of microalbuminuria increases with increasing grades of obesity. So this proves that increasing grades of obesity is an independent risk factor for microalbuminuria.

WHR & MAU

Next we analysed the significance between WHR & microalbuminuria separately among the male & female cases. The acceptable WHR for male & female was different, hence this analysis.

The acceptable WHR for males was <0.90 , hence among the male cases 2 were within acceptable limits , & the rest 24 were in the unacceptable range. The prevalence of microalbuminuria was 0 among 2 acceptable cases, 7 among 24 unacceptable cases.

The p value for this association was >0.05, which was not significant. So the correlation between WHR & microalbuminuria among male obese persons was not significant.

Even though the prevalence of microalbuminuria among unacceptable male persons was high it was not statistically significant, so it should be merely by chance only.

Next among female cases the acceptable WHR was <0.80. In this study there were 3 acceptable & 21 unacceptable female cases. Among the 3 acceptable cases none had microalbuminuria, & among the 21 unacceptable cases 9 had microalbuminuria.

The p value for this association was >0.05 , so it was statistically not significant. Though only unacceptable cases had

microalbuminuria among the female cases, it should be by mere chance only according to this study.

So from this study there was not much correlation between WHR & microalbuminuria among both female & male cases, though microalbuminuria was present only in the unacceptable cases.

But to exactly define the correlation between WHR (which is indicative of visceral adiposity) among obese persons & microalbuminuria we have compare equal no of acceptable & unacceptable cases & assess its statistical significance.

WC & MAU

Now we want to assess the strength of correlation between WC & microalbuminuria among the cases.

For the male obese cases , < 102 cms is taken as the acceptable limit of WC. In this study among the male cases there were 20 acceptable & 6 unacceptable cases based on the WC.

Among 20 acceptable male cases 2 had microalbuminuria & among 6 unacceptable cases 5 had microalbuminuria. The p value for this association was <0.001, which was highly significant. Hence there is a strong correlation between WC & microalbuminuria among male

cases. So the male cases who had unacceptable WC had high prevalence of microalbuminuria among them.

So for the female obese cases the acceptable WC was <88 cms. Hence in this study there were 7 acceptable female cases & 17 unacceptable female cases based on the WC. Among 7 acceptable cases 2 of them had microalbuminuria & among 17 unacceptable cases 7 had microalbuminuria.

The p value for this association was >0.05 , so it was statistically not significant. So there is no direct correlation between WC & microalbuminuria among the female cases in this study.

So in this study , microalbuminuria has a stronger association with obesity independent of the risk factors like diabetes, hypertension & dyslipidaemias.

Hence obesity itself with increasing grades of BMI is an independant risk factor for microalbuminuria.

Evaluation of microalbuminuria is recommended as a screening tool for all obese persons , in particular with reference to increasing grades of BMI, to assess the future risk of both kidney disease & cardiovascular disease.

Therefore urinary screening for microalbumniuria atleast once in a year is a must for all obese persons to prevent the development of future complications.

Heightened awareness of microalbuminuria as an early marker of endothelial dysfunction, makes it as an essential screening tool in all obese persons atleast once in a year.

CONCLUSION

1) In this study of 50 cases & 50 controls, the prevalence of microalbuminuria was found to be high among the obese persons.
2) The prevalence of microalbuminuria in obese persons was statistically high in correlation with the increase in severity of obesity , based on BMI.
3) The prevalence of microalbuminuria was high among both male & female cases with increase in WHR, but was not statistically significant.
4) The prevalence of microalbuminuria was high among male cases with increased WC and it was highly statistically significant.
5) The prevalence of microalbuminuria was high among female cases with increased WC but it was not statistically significant.
6) Therefore urinary screening for microalbuminuria in all obese persons should be done, to prevent the development of future complications like cardiovascular & renal disease.

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PROFORMA

NAME: AGE: SEX:

ADDRESS: OCCUPATION:

OP NO:

PRESENT HISTORY: (NATURE OF COMPLAINTS)

PAST HISTORY:

HTN: DM: CAD:

COPD: CKD: TB:

PERSONAL HISTORY:

SMOKING: ALCOHOLISM: DRUG ABUSE:

FAMILY HISTORY:

HTN: DM:

ANTROPOMETRY:

HEIGHT: WEIGHT: BMI:

WAIST CIRCUM: HIP CIRCUM: WHR:

GENERAL EXAMINATION:

FUNDUS: THYROID:

XANTHELASMA: ACANTHOSIS NIGRICANS

FEATURES OF CUSHING'S SYNDROME:

VITALS:

PULSE RATE: BLOOD PRESSURE:

RESPIRATORY RATE: TEMPERATURE:

SYSTEMIC EXAMINATION:

CVS: RS:

ABDOMEN: CNS:

INVESTIGATIONS:

BLOOD GLUCOSE: SERUM UREA:

SERUM CREATININE: TOTAL CHOLESTEROL:

URINE – MACROALBUMINURIA (DIPSTICK):

URINE – SUGAR:

URINE – DEPOSITS:

ECG IN ALL LEADS:

MICROALBUMINURIA: SPOT URINE ALBUMIN CREATININE RATIO (UACR):

ABBREVIATIONS

ACEI – Angiotensin converting enzyme inhibitor

ADA – American diabetes association

ARB – Angiotensin receptor blocker

BIA – Bioelectrical impedance analysis

BMI – Body mass index

BP – Blood pressure

CVD – Cardio vascular disease

CT – Computed tomography

DM – Diabetes mellitus

ESRD – End stage renal disease

FSGS – Focal segmental glomerulosclerosis

GFR – Glomerular filtration rate

HC – Hip circumference

HT – Height

HTN - Hypertension

LDL – Low density lipoprotein

MAU – Microalbuminuria

PAI-1 – Plasminogen activator inhibitor-1

RAS – Renin angiotensin system

RBS - Random Blood Sugar

TGF-β – Transforming growth factor-β

TGL – Triglyceride

TNF-α – Tumor necrosis factor-α

UACR – Urine albumin creatinine ratio

UAE – Urine albumin excretion

VAT – Visceral adiposity

WC – Waist circumference

WHR – Waist hip ratio

WT - Weight